COCA Call: It's a Small World After All: Dengue and Malaria in U.S Residents - Recognizing and Treating These Mosquito-borne Diseases
Date/Time: June 9, 2010 (2:00 PM- 3:00 PM ET)
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Coordinator: Welcome and thank you for standing by. For today's conference all parties will be on listen-only. During the question and answer portion please press star 1 to ask a question, you will be prompted to record your name. Please unmute your phone and record your name clearly in order to be introduced with your question.

Today's conference is being recorded, if you have any objections you may disconnect at this time. I will now turn today's call over to Loretta Jackson-Brown. Thank you, you may begin.

Loretta Jackson-Brown: Thank you (Denise). Good afternoon. I'm Loretta Jackson-Brown and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Communication System at the Centers for Disease Control and Prevention.

I am delighted to welcome you to today's COCA conference call. It's a Small World After All, Dengue and Malaria in U.S. Residents - Recognizing and Treating These Mosquito-borne Diseases.

We are pleased to have Dr. David Townes, Epidemic Intelligence Service Officer with CDC Malaria Branch and Dr. Christopher Gregory, Epidemic Intelligence Service Officer with CDC Dengue Branch with us today to discuss the evolving epidemiology of the two most prevalent mosquito-borne diseases, malaria and dengue.

During today's call you will hear the presenters referring to slides in their PowerPoint presentation. The PowerPoint slide set is available from our COCA Website at emergency.cdc.gov/coca. Click on Conference Calls, the slide set can be found under the call in number and passcode.

The objectives for today's call are that participants will be able to describe evolving epidemiology of the two most prevalent mosquito-borne diseases worldwide, compare and contrast clinical presentations of dengue and malaria, describe prevention strategies for dengue and malaria, identify key points and diagnosis in treatment for dengue and malaria, discuss the importance of reporting suspected cases of dengue or malaria and reporting protocol.

Following the presentation you will have an opportunity to ask questions of our two presenters. Dialing star 1 will put you into the queue for questions.

In compliance with continuing education requirements all presenters must disclose any financial or other relationship with the manufacturer of commercial products, suppliers of commercial services or commercial

supporters as well as any use of an unlabeled product or products under investigational use.

This presentation will not include any discussion of the unlabeled use of product or products under investigational use. CDC, our planners and our presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services or commercial supporters. There is no commercial support for this presentation.

Our first presenter this afternoon is Dr. Townes. Dr. Townes is a Lieutenant Commander in the Commissioned Corp of the U.S. Public Health Services. He is an Epidemic Intelligence Service Officer and Medical Epidemiologist in CDC's Malaria Branch Centers for Global Health.

He holds a diploma in tropical medicine and hygiene from the Royal College of Physicians, London School of Hygiene and Tropical Medicine University of London, London England. Dr. Townes recently served as the Principal Investigator, Malaria Assessment and Development of Surveillance in post-earthquake Haiti.

Dr. Townes currently is on leave from University of Washington School of Medicine, Division of Emergency Medicine and the University of Washington Medical Center Seattle, Washington where he is an Associate Professor of Medicine and attending physician.

Our second presenter this afternoon is Dr. Gregory. Dr. Gregory is an Epidemic Intelligence Service Officer in CDC's Dengue Branch, National Center for Emerging and Zoonotic Infectious Diseases, San Juan Puerto Rico.

In this role he conducts outbreak investigation, program evaluation, study design and management, statistical analysis and healthcare provider education. Dr. Gregory is a pediatrician. He completed his pediatric residency, international health track, at Rainbow Babies and Children's Hospital, Cleveland, Ohio and Pediatric Critical Care Fellowship Children's Hospital of Denver, Denver, Colorado.

If you're following along on the slides you should be on Slide 6. Please join me in welcoming our first presenter. Dr. Townes.

Dr. David Townes: Thank you Loretta. Good afternoon everyone. As Loretta said we should be on Slide Number 6. Over the next 20 minutes I'm going to discuss malaria and travel. The next slide is an outline for today's discussion. We will start with a review of the some of the basics of malaria pathophysiology and epidemiology.

We'll then discuss malaria and international travel followed by a review of malaria prevention, diagnosis and treatments. Finally I will present what I hope are some useful resources related to the topic of malaria and travel.

Malaria is caused by a parasitic infection with a protozoan from the genus Plasmodium. There are five species that cause pathology in humans including falciparum, the most severe form as well as vivax, ovale, malariae and finally knowlesi which is an infection of old-world monkeys in Southeast Asia primarily the island of Borneo. It has been shown to infect humans and cause clinical disease.

On the next slide you'll see a map of where malaria is endemic. It's endemic in over 100 countries with approximately half the world's population at risk. The vector is the female anopheles mosquito. There are 400 different species, 30 of which are considered important for malaria transmission. They are primarily night-biting with some resting indoors and some outdoors after feeding.

The next slide demonstrates the basic malaria vector host relationship. When a person infected with malaria, shown here in the upper left, is bitten by an uninfected mosquito that mosquito becomes infected with the malaria parasite as shown on the right side of this diagram.

If that now infected mosquito goes on to bite a person not infected with malaria, shown here on the lower left, they may become infected with malaria thus completing the cycle.

With that background look at the next slide, let's examine the life cycle of the malaria parasite. The lifecycle is divided into the mosquito stage, the human liver stage and the human blood stage. It's helpful to keep this malaria parasite lifecycle in mind when we discuss prophylaxis. As the point of action of each medication used in prophylaxis in the lifecycle influences its dosing regimen.

In the mosquito stage, shown on the next slide, the mosquito takes a human blood meal and injects the gametocyte form of the parasite. These mature into sporozoites within the mosquito and when the mosquito subsequently bites another human sporozoites are injected into that individual infecting them with malaria.

In the human liver stage, shown on the next slide, the malaria parasite enters liver cells of a recently infected individual forming tissue schizonts. Some medications work on the tissue schizont form of the parasite. These tissue schizonts eventually rupture and the parasite subsequently infects red blood cells in the human stage shown on the next slide.

This form of the parasite is known as the blood schizont form. As the parasite develops within red blood cells some will cause the red blood cells to rupture and subsequently infect additional red blood cells and continue the cascade of infection of red blood cells.

Some medications work on the human blood stage form of the parasite or the blood schizont form. Some parasites will not develop into blood schizonts rather they will develop into gametocytes as shown on the next slide.

These gametocytes will eventually be taken up by a biting mosquito starting the cycle all over again. Some of the medications as we will see work on the gametocyte form of the parasite.

On the next slide we see the lifecycle with the liver circled. Up until now the lifecycle has been essentially the same for all species of plasmodium. However in infections with plasmodium vivax and plasmodium ovale some of the parasites in the liver will enter a dormant form called hypnozoites.

These hypnozoites may stage dormant for many months until they are released from the liver at a later time causing clinical malaria. This is called relapse. We will discuss this later. Some medications work on the hypnozoite form of the parasites.

I think it's important to understand the true worldwide burden of malaria. Every year there are about 250 million cases of malaria resulting in approximately 880,000 deaths. Over 90% occur in sub-Saharan Africa with the majority of deaths in children under five years of age.

Let's now take a look at malaria and international travel. What are the risks to the international traveler? Well for every 100,000 individuals visiting a developing country for one month about half will become ill. The majority of these will have self-limited gastrointestinal problems including traveler's diarrhea.

About 8% will see a physician and 5% will have to alter their activities and stay in bed. Only 1 in 100,000 will die from an infectious disease such as malaria. The greatest potential life threat to the international traveler is still far and away motor vehicle accidents.

This graph depicts malaria cases, shown by the gray bars, and deaths, shown in red, in the United States between 1985 and 2008. As you see there are roughly 1500 cases of malaria reported in the United States each year with a handful of deaths.

The next slide contains a chart that depicts the geographic area of acquisition of malaria cases imported into the United States in 2008. Almost 44% were acquired in Africa and 13% in Asia. In almost 39% of cases, however, the geographic area is unknown. This is a result of incomplete reporting.

In terms of doing a travel risk assessment all travel is not created equally. Geography alone is not enough. Risk assessment must be individualized. Not

all travelers to the same country will have the same risks; it will depend on the destinations and the specific itinerary.

For instance someone going to climb Mt. Kilimanjaro in Tanzania has a very different risk profile compared with someone going to Tanzania for a safari. The type of travel, activities and the combinations will also influence risk. A business traveler staying in a four-star hotel in a capital city has a different risk profile than a humanitarian relief worker staying in the field.

In many parts of the world malaria is seasonal and risk varies considerably with time of year and amount of rain. Finally, one must consider individual risk factors such as pregnancy or the chance of pregnancy which will affect recommendations for travel and prophylaxis.

Moving onto prevention let's now take a look at options for malaria prevention. Prevention basically falls into two categories, mosquito avoidance including insect repellants, protective clothing and bed nets and chemo-prophylaxis with medications.

The next slide discusses mosquito avoidance. There is some confusion about insect repellants and the significance of the concentration of DEET. There is no additional benefit to DEET concentrations over 50% so the use of preparations with 100% DEET is really unnecessary.

The concentration of DEET really affects the duration of effectiveness rather than overall effectiveness. Between 20% and 50% DEET concentration the lower concentrations are just as efficacious but require more frequent application.

One alternative to DEET is Picaridin. In concentrations of at least 20% Picaridin has similar efficacy to DEET. Other options include oil of lemon eucalyptus and IR3535.

Additional mosquito avoidance measures include Permethrin-treated clothing. Permethrin is available to the consumer both as a spray and in pre-treated clothing. It is also important to sleep under an insecticide treated bed net or ITN or a long lasting insecticide treated bed net or LLIN.

The next slide has a table that shows some common medications used for prophylaxis and the form of the parasite on which they act. Thinking back to the parasite life cycle as you can see all of the medications work on the blood schizont form.

Malarone also works on the tissue schizont form and Primaquine works on all forms of the parasite giving it a unique role in prophylaxis in certain situations.

Let's now talk about each medication individually. Chloroquine was the mainstay of prophylaxis for years but widespread P. falciparum resistance has limited its use. There are limited exceptions where P. falciparum is still sensitive, Haiti is one example.

Chloroquine is started one to two weeks before travel, taken weekly, and because it works on the blood schizont stage of the parasite it must be taken until four weeks after travel.

Mefloquine has a reputation for psychological side effects and should be avoided when possible in patients with a history of seizures, sleep disturbance and psychiatric disease.

People taking Mefloquine often report very vivid dreams. Similar to Chloroquine it is started two weeks before travel and taken weekly. And again because it works on the blood schizont stage it is taken until four weeks after travel.

Doxycycline is a popular choice because it is inexpensive and it does offer protection against other diseases including leptospirosis and tick-borne diseases such as scrub typhus.

Some people experience gastrointestinal intolerance with Doxycycline but this is generally a problem with the generic or (hyclate) form of the drug. The monohydrate form is often better tolerated. It is started one to two days before travel, taken daily and likely Chloroquine and Mefloquine is taken until four weeks after travel.

On the next slide we'll discus Malarone which is a combination of Atovaquone and Proguanil. It tends to be expensive but is often the best choice for short trips. It is started one to two days before travel and taken daily until seven days after travel.

Remember Malarone not only works on the blood schizont form of the parasite just like Chloroquine, Mefloquine and Doxycycline but also on the tissue schizont form. By working on this earlier stage of the parasite before it enters the blood stage Malarone only needs to be taken for seven days after leaving an endemic area.

Finally Primaquine, Primaquine works on both the blood schizont and tissue schizont form of the parasite so like Malarone Primaquine only requires a seven day course after leaving an endemic area.

In addition because Primaquine works on the hypnozoite form of the parasite it is used in P. vivax and P. ovale infections to eliminate hypnozoites dormant in the liver. This is called terminal prophylaxis. Primaquine is contraindicated in individuals with G6PD deficiency as it make cause hemolysis.

We'll now move onto diagnosis. You should be on the outline slide with Diagnosis highlighted. The mainstay of malaria diagnosis is microscopy namely a thick and thin blood smear.

A thick blood smear generally answers the question malaria? Yes or no. It is especially useful with low parasitemia that might be missed on a thin smear. If negative it should be repeated every 12-24 hours for 36-72 hours until positive or until three blood smears have been performed.

A thin blood smear also answers the question malaria: Yes or no. And in addition is also helpful in determining the plasmodium species and the level of parasitemia which is the percentage of red blood cells that are infected. It should be repeated every 12-24 hours until positive or until three smears have been performed. There are other diagnostic modalities but the mainstay of diagnosis remains microscopy.

Moving onto treatment, you'll notice as we discuss treatment that some of the drugs used for treatment are the same as those used for prophylaxis. Factors

guiding treatment include plasmodium species, the geographic area of acquisition, drug resistance patterns and the clinical status of the patient.

Patients with uncomplicated malaria often have fever, chills and headache. They might also complain of body aches, vomiting, diarrhea and cough. Uncomplicated malaria is generally treated with oral therapy.

Artemisinins are a new class of anti-malarials derived from the sweet wormwood shrub, a plant used medicinally in China for thousands of years. Artemisinins are combined with a second drug as Artemisinin combination therapy. This is the World Health Organization's first line treatment for uncomplicated malaria.

In the United States one formulation is available, Coartem, first FDA approved in 2009. Coartem is a combination of Artemether and Lumefantrine. It is used in infections with P. falciparum or when the species is unknown. Treatment is a three-day course. Malarone may also be used for infections with P. falciparum or when the species is unknown. Like Coartem it is a three-day course.

Moving onto Quinine, Quinine may also be used in infections with P. falciparum or when the species is unknown. It is used in combination with either doxycycline, tetracycline or clindamycin. It is either a three-day or seven-day course depending on the geographic location of the malaria acquisition.

Mefloquine may be used in infections with P. falciparum or when the species is unknown however it should not be used for P. falciparum acquired in Southeast Asia. It is a one-day course.

Moving onto Chloroquine, Chloroquine may be used in infections with P. vivax when they are not acquired in Papua, New Guinea or Indonesia. It also may be used in areas where P. falciparum is known to still be sensitive such as Haiti. It is a two-day course.

Finally Primaquine may be used to eradicate hypnozoites in known P. vivax or P. ovale infections. A common scenario is a patient who had malaria several months ago and was treated but now presents with malaria again without any recent travel.

Likely they were treated for their primary malaria but not for the hypnozoite form of the parasite and are now having relapse due to the release of these hypnozoite forms. Primaquine is a 14-day course. One must test for G6PD deficiency prior to administering Primaquine as it may cause hemolysis.

You should now be on the slide that discusses severe malaria. Severe malaria is associated with severe anemia, acidosis, renal failure, ARDS, hemolysis, shock, cerebral malaria and parasite densities of greater than 5%. Patients with severe malaria should be treated with IV therapy.

IV Quinine - pardon me, IV Quinidine plus either doxycycline, tetracycline or clindamycin may be used. Another choice is Artesunate, an IV form of Artemisinin which is available in the United States through the CDC via an investigational new drug protocol. Artesunate is a three-day course followed by a course of a second drug.

Finally the CDC offers a variety of very helpful resources for the prevention and treatment of malaria. The CDC Website includes a malaria Webpage and

a traveler's health Webpage which contain good general information about travel and malaria.

The malaria map application offers specific geographic information about malaria risks. Malaria is a nationally reportable disease in the United States and should be reported to the state health department. The surveillance reporting form is also available online.

The CDC Yellow Book contains easy to use tables and country-specific information for malaria risk and prophylaxis. It is available both in hard copy and online.

And finally the CDC treatment table is an excellent resource for the treatment of malaria and is also available online. There is also a malaria hotline for clinicians to call 24 hours a day to discuss cases of malaria or potential cases of malaria. Thank you.

Loretta Jackson-Brown: Thank you Dr. Townes. Please welcome our next presenter, Dr. Gregory.

Dr. Christopher Gregory: Thank you Loretta. We will start on Slide Number 55 and I'll begin with a brief overview of dengue. Dengue is a single strand of RNA virus in the flavivirus family which also includes the West Nile, Japanese encephalitis, and yellow fever viruses.

There are four serotypes of dengue named Dengue 1-4. Each serotype is capable of causing illness ranging from asymptomatic cases to life threatening infections. Infection with one serotype confers lifelong serotype specific immunity so an individual can have dengue up to four times in their life.

On the next slide we see the burden of disease. Forty percent of the world's population lives in dengue-endemic areas including over 4 million U.S. citizens, mostly those residing in Puerto Rico.

An estimated 50-100 million cases of dengue occur annually worldwide and cases in the Western Hemisphere have increased substantially in the past 20 years. Dengue is now the leading cause of acute febrile illness in U.S. travelers returning from Asia, South America and the Caribbean.

On slide 59 we have a map showing the extent of dengue as of 2006. Red dots indicate areas with newly emergent or re-emergent dengue transmission from 2000-2006. Since 2006 dengue has spread to include additional parts of Saudi Arabia, Mauritius and Cape Verde.

While historical description of apparent dengue outbreaks exist dating back to at least the 18th Century the second half of the 20th Century showed remarkable growth in the numbers and severity of dengue cases.

Several factors contributed to this growth, increased industrialization led to an increase in the number of artificial containers able to function as mosquito breeding sites. Rapid population growth and urbanization increased the ease and force of disease transmission. And the ease and speed of international travel allowed dengue infected individuals to rapidly introduce dengue into new areas.

Starting in the 1950s epidemics of the more severe form of dengue, dengue hemorrhagic fever, were seen in many large Southeastern Asian cities. And by

1970s dengue was the leading cause of hospitalization and death in children in this area.

As seen in this figure on Slide 61 beginning in the early 1980s cases of dengue in the Western Hemisphere have also dramatically increased. Dengue transmission, dengue is primarily transmitted by the bite of an infected adult female Aedes mosquito.

After the virus is required via mosquito it must incubate for 8-12 days in the mosquito before being transmissible; the so-called extrinsic incubation period. The mosquito subsequently remains infected for life. The typical life span of a mosquito in the wild is around two weeks to a month for an Aedes mosquito.

The virus is able to be transmitted to humans by a mosquito bite containing as few as 100 viral particles. Incubation period in humans is 3-14 days. The virus is present in the blood for around 24 hours before the patient becomes febrile. And patients are viremic for five to six days which usually correlates with the time the patient is febrile.

Asymptomatic infections are common in children and individuals with primary infections. Studies in blood donors have shown that individuals with asymptomatic infections have viral loads as high as symptomatic patients.

On Slide 65 we have other routes of transmission of dengue. Dengue has been documented to be transmissible by organ or tissue transplantation, blood transfusion and occupational exposure to blood. During high transmission periods in dengue-endemic areas as many as 1 out of every 600 blood products contain dengue virus.

Vertical transmission of dengue can also occur either in utero or at parturition but little data exists to estimate the true incidence of this occurrence. Cases reported in the literature have consisted solely of symptomatic infections in the neonate after symptomatic infection in the mother late in the course of pregnancy.

Mosquito vectors, Aedes aegypti is a more efficient vector than Aedes albopictus. This mosquito lives in and around human habitations spending the majority of time in dark areas such as closets or under furniture, usually bites indoors and during the day and lays eggs preferentially in relatively clean water in artificial containers.

Aedes albopictus partially because it is not as fastidious and will also feed on other animals is a less efficient vector but was responsible for an outbreak in Hawaii in 2001. With few exceptions recent large scale efforts of vector control of the Aedes mosquito have been unsuccessful.

On Slide 69 we have pictures of the Aedes albopictus and Aedes aegypti before and after feeding. Both of these mosquitoes have characteristic white markings or light stripes on their legs.

Now I'll talk a little bit about the risk of acquiring dengue in the United States. For local transmission of dengue four elements are needed, a largely susceptible population, ample mosquito vectors, the introduction of the virus into the area and sufficient opportunity for mosquito human interactions. All these factors are present in many sub-Tropical regions of the U.S.

It is not surprising then that since 1980 several outbreaks have occurred in the U.S. including seven outbreaks in the Texas Mexico border region, an outbreak in Hawaii in 2001 and most recently an outbreak in Florida.

Aedes Aegypti and Aedes albopictus are found in many of the warmer parts of the U.S. and have been gradually expanding their territories. Increased travel and immigration between the U.S. and dengue-endemic countries has led to an increase in the number of travel-associated dengue cases.

Many of these travelers will return to the U.S. while viremic and therefore potentially capable of transmitting the virus to local mosquitoes. On Slide 73 we show the known distribution of Aedes aegypti in the U.S. as of 2005. And on the following slide how Aedes albopictus has expanded its range in the United States since it was first identified here in 1985.

Clinical presentation of dengue, in the new World Health Organization dengue guidelines that came out in November of 2009 increased emphasis was placed on recognizing that the most important feature that differentiates severe and non-severe dengue cases is actually increased vascular permeability rather than hemorrhage.

Indeed the WHO has moved away from using the potentially misleading term DHF or Dengue Hemorrhagic Fever due to the fact that both severe and non-severe dengue can have bleeding manifestations.

Dengue treatment, as no effective antiviral or vaccine currently exists for dengue the standard of care is supportive management based on the appropriate use of IV fluid therapy when needed.

Accumulating clinical experience with the management of dengue and the development of best clinical practices has reduced the case fatality rate to much less than 1% even in the most severe cases. This contrasts with early mortality rates in excess of 30%-40%.

The clinical course of dengue follows a relatively stereotypical pattern. The illness begins abruptly and is divided into three phases, the febrile, critical and recovery phases.

As seen on Slide 79 the febrile phase typically lasts 2-7 days. When the fever resolves patients enter into a critical phase of 24-48 hours when patients will either improve or deteriorate.

Those that deteriorate will usually manifest warning signs and is therefore essential that clinicians are especially vigilant during this time period. Fever that lasts greater than seven days is unusual and should prompt an investigation for other causes of fever.

The onset of the critical phase as seen on the next slide can usually be identified by defervescence, a drop in the white blood cell count followed by a drop in the platelet count often associated with a rise in the hematocrit and the development of warning signs in those with severe infections.

These warning signs include severe abdominal pain, persistent vomiting, developing of ascites or pleural effusion, mucosal bleeding, lethargy or restlessness and liver enlargement.

These warning signs are the result of plasma leakage due to vascular permeability and often indicate the presence of a compensated shock state in the patient.

This plasma leak is time limited lasting only for 24-48 hours and clinicians must be careful to watch for the resolution of this phase and the start of the recovery phase to avoid iatrogenic fluid overload.

The recovery phase, as shown on Slide 82, is the time when extravascular fluid is reabsorbed over a period of 48-72 hours and can be recognized by an overall improvement in patient status and hemodynamics and the onset of spontaneous diuresis.

During this phase the hematocrit normalize or decrease and the white blood cell count will increase which will be followed by an increase in the platelet count.

Common clinical problems include dehydration and febrile seizures in the febrile phase, shock, hemorrhage and organ dysfunction in severe cases in the critical phase and fluid overload in the recovery phase.

Common laboratory findings include leucopenia and a relative lymphocytosis often with atypical lymphocytes towards the end of the febrile phase, thrombocytopenia and hemo concentration around the time of defervescence and mildly to moderately elevated transaminases.

I'll now talk a little bit about dengue diagnosis and reporting. On Slide 86 is the differential diagnosis of dengue. Dengue can be difficult to distinguish clinically from many other infections including common seasonal illnesses

such as influenza and enterovirus as well as other tropical diseases such as leptospirosis, malaria and typhoid. Severe cases are often initially diagnosed as bacterial sepsis.

For this reason laboratory confirmation should be sought when possible however these results are seldom available in time to guide clinical management.

Diagnosis can be confirmed by detection of virus within the first five days of illness by polymerase chain reaction or detection of the dengue protein non-structural-1 where this test is available.

After day five when viremia is unlikely to be present PCR is not useful and diagnosis rests on detection of dengue IgM antibodies. These antibodies can persist for up to three months and in dengue-endemic areas only indicate recent dengue infection rather than current infection.

IgG antibody tests are not useful for clinical diagnosis as they remain elevated for lifetime against - after infection and frequently cross-react with antibodies against other flaviviruses.

Dengue was made a nationally notifiable disease in 2009 although not all states with Aedes mosquitoes currently mandate reporting. Dengue cases should be initially reported to the appropriate state and local health department.

The fact that the recent outbreak in Florida was detected thanks to physician notification in New York State highlights the importance of properly reporting cases.

Contact information, please check out our Website at www.cdc.gov/dengue for general guidance on dengue or wwwnc.cdc.gov/travel for guidance as it relates to the international traveler. The phone numbers and fax numbers for the dengue branch are also included on this slide. Thank you.

Loretta Jackson-Brown: Thank you Dr. Townes and Dr. Gregory for that informative presentation. We will now open up the lines for the question and answer session.

Coordinator: Thank you. And at this time if you would like to ask a question please press star 1 on your touchtone phone. Once again star 1 if you would like to ask a question. You will be prompted to record your name. Please unmute your phone and record your name clearly in order to be introduced at the conference.

One moment please for the first question. The first question comes from Dr. (Rocke), your line is open.

Dr. (Rocke): Thank you. I have two or three questions actually really quick. One is a comment. Doxycycline noted side effects there I would include a sun sensitivity sort of dermatitis that can occur with doxycycline as well that should be considered especially since people that are taking this for malaria would probably be in a fairly sun-exposed area.

Question about the Quinine pronunciation, Quinine, is that just a regional pronunciation or is that the way it's pronounced these days? A comment about Skin-So-Soft, originally the urban legend was that Skin-So-Soft by itself prevented mosquito bites and then eventually the company decided to add

DEET to its product so that it would in fact prevent mosquito bites to some extent. And I assume that was implied by the 10%-20% that was noted next to it.

And then my final real question is where is the latest information on where the Aedes mosquitoes are in the United States; more recent information than 2005? Thanks.

Dr. David Townes: Well it sounds like the first couple are related to malaria and then the second part of the question is sort of directed more towards dengue so I'll touch base with the - touch the first.

First of all your comment about doxy is excellent. I basically at the time did not - was not able to go over all of the side effects and potential complications but you're absolutely right that taking doxycycline does put people at risk for sun sensitivity. And as you pointed out most of the people that are taking doxycycline for malaria are often in sunny, sunny areas so that's an excellent point.

In terms of Quinine versus Quinine I don't know I've heard it - that's a great, great question. Actually I'll have to look into that area but I don't know what the current - I hear people pronounce it both ways and I think I've been guilty of pronouncing it both ways myself. So, maybe if anyone in the audience does know the origin or the regional differences that would be great but I actually do not know.

And in terms of the IR3535 Skin-So-Soft, yeah, the Avon who was the original producer of Skin-So-Soft and may still be I don't know, promoted it

as an effective mosquito repellent and then initial studies showed it really did not work as you pointed out.

And the preparation with IR3535 in concentrations of 10% to 20% has been shown to work. And I think there's actually a concentration that just has IR3535 and does not contain DEET and that actually is effective by itself. So that's why I offer it as a possible alternative to DEET.

I'm fairly sure that there is a formulation now that just has IR3535 and does not have DEET. So when I was - when I listed the 10% to 20% concentration that was actually of the ingredient IR3535 not DEET. So I hope that sort of addresses your questions. And I'll turn it over to Chris to discuss the distribution of mosquitoes.

Dr. Christopher Gregory: Yes, thank you. This is Dr. Gregory from the Dengue Branch. So, yes, it's actually a little bit difficult to find the nationwide sort of the most up to date distribution of the Aedes mosquito. It tends to be somewhat regionalized and to my knowledge there aren't a lot of national organizations that kind of sort of compile all the reports from the various vector control programs.

I mean, the American Mosquito Control Association are probably the best place to try and find that information that's more recent. The slides I have came from Colorado State University. And also the other comment about sort of this is with the Aedes sort of the absent of evidence of the mosquito in some of these counties shouldn't be taken as evidence that - of absence of the mosquito.

I mean, if you look at the map sort of especially for albopictus or for aegypti you can see that there's some counties which look like the mosquito is absent or - but actually all those gray spaces are where they're not reported. And so you can see at the - for an example on the bottom of Florida, you know, Miami County there's no Aedes reported although, you know, in the surrounding counties they all have Aedes albopictus and Aedes aegypti.

And there's some other places like that so it should be taken with a little bit of a - sort of a broad overview as opposed to sort of specifics that you can really trust that if it's not shown on the map it doesn't exist there. Thank you.

Coordinator: And are you ready for the next question?

Loretta Jackson-Brown: Yes please. Thank you.

Coordinator: It comes from (Gayle Russelo), your line is open.

(Gayle Russelo): Good afternoon. Thank you so much. This has been a terrific program and the slides are wonderful. I have one question for both presenters. With regards to Skin-So-Soft seeing this here I can imagine - I do travel health and I can imagine my travelers going to jump on this.

So I'd just like clarification further because (Frayden and Day) and I know that that was a New England article of a while back but they had said yes it was effective but only for nine minutes. So I'm wondering about the duration of protection with this new 10%-20% concentration.

And then my second question is what about progress with a dengue vaccine?

Dr. David Townes: Maybe, Chris, you want to go ahead and start with this one; we'll do them in the reverse order?

Dr. Christopher Gregory: Sounds good. So, you know, there's at least five candidate vaccines in development. Obviously the tricky thing with developing a dengue vaccine is you have the four serotypes. And we didn't really get into this too much but there's this hypothesis of (anti dependent) enhancement.

And so it's actually usually people's second infection where they get really sick. And so one of the things that has been slowing down vaccine development in addition to just making sure all the safe and immunogenic is to make sure that you get good coverage against all four serotypes simultaneously so you don't set people up with vaccination if protection wanes and then if they get a natural infection to get more severe disease.

There are at least one or two candidate vaccines that are entering Phase 3 trials at this point in time. But probably, you know, several years away still before anything is available on the market.

(Gayle Russelo): Thank you.

Coordinator: The next question comes from (Joe) - oh I'm sorry, go ahead.

Dr. David Townes: I think she - I think (Gayle) also had a question about...

(Gayle Russelo): ...a question about the duration of protection, yeah.

Coordinator: Go right ahead.

Dr. David Townes: Yeah, you know, so about the duration of IR3535 which is the active ingredient in one formulation of Skin-So-Soft. And, you know, I don't think this has been exceptionally well studied. I know that the study you're talking about - there's another one that they looked at and they found that IR3535 that - Avon Corporation's IR3535 repellant provided an average duration of about 23 minutes and the range in that study was 10-60%.

So it's a little bit tricky. I think that, you know, I think that DEET-based products are probably still the way to go and what I recommend travelers use. There are certainly people that don't like DEET because of the sort of chemical feel, the chemical smell. And as you know it can be very toxic to certain plastics and nylon, some Gore-Tex jackets, watch - plastic watch bands it can actually be...

((Crosstalk))

Dr. David Townes: ...quite toxic. So for people like that that are going to take - use the Skin-So-Soft I don't think, you know, the CDC recommends it in that it's been shown to be an effective repellant. But in terms of reapplication times, you know, I think it almost takes a little individual experimentation. But you're right, it's certainly shorter than DEET.

You know, DEET in 50% concentrations will last for 8, 10, 12 hours.

(Gayle Russelo): Sure, sure.

Dr. David Townes: And I think that Skin-So-Soft you're probably looking at having to reapply it every hour or so.

(Gayle Russelo): Okay thank you. That's very helpful.

Dr. David Townes: Okay, okay, thanks.

(Gayle Russelo): Thanks very much.

Coordinator: And you're ready for the next question then?

Loretta Jackson-Brown: Yes, (Denise), go ahead.

Coordinator: All right, that comes from (Joe Var), your line is open.

(Joe Var): Hi, this is for Dr. Townes. We have an international travel program for some of our businessmen here and they often go to either Manila or Mumbai. My question is regarding the malaria that Manila, if they're just going to stay in the city it says on the (trip med) Website that they really don't need the Malarone medication but if they're going to go out sight seeing or out in the country then they do.

The second question that I have is what if they stay for a lengthy visit for say six months, is Malarone still indicated for that whole time?

Dr. David Townes: So you're talking about the Philippines, correct?

(Joe Var): Well both, I mean, for Manila and if they had a six-month visit in Mumbai.

Dr. David Townes: Well first of all for the Philippines there's really not a lot of malaria in the urban areas so for travelers who are going to just stay in an urban area and I

think that's no prophylaxis is indicated. If they're going to be in the rural areas then obviously they need some.

The business traveler going to a meeting in Manila, staying in a hotel I don't think they need to use anything. In terms of traveling to Mumbai for longer-term or in the rural Philippines for longer-term, you know, there have been experiments with Malarone for several months; I think that's okay.

But, you know, then I would probably go to something - one of the weekly medications; you could use Mefloquine, you could actually use - well doxy is daily but Doxycycline or Mefloquine would probably be alternative choices.

(Joe Var): Alright thank you.

Dr. David Townes: Sure.

Coordinator: And the next question comes from (Robert Desmond), your line is open.

(Robert Desmond): Hi, thank you. (Gayle) just asked the question that I had namely dengue vaccine so you've covered that, thank you.

Coordinator: The next question comes from (Michelle Waters), your line is open.

(Michelle Waters): Thank you. My question concerns the geographic distribution of the serotypes, is there one or at any given area could you find all for serotypes? Is there any relationship to the mosquito vector?

Dr. Christopher Gregory: In some of the dengue serotypes you definitely can find all serotypes circulating in the same area. And that's actually interesting because

when you have hyper-(endemnicity) sort of of three or more serotypes circulating at the same time then you tend to have larger outbreaks and more severe disease going on.

And there doesn't seem to be any relationship between the mosquito vector and the serotype. Either vector is able to transmit any of the serotypes.

(Michelle Waters): Thank you.

Coordinator: I have no other questions at this time.

Loretta Jackson-Brown: Okay thank you (Denise). On behalf of COCA I would like to thank everyone for joining us today with a special thank you to our presenters, Dr. Townes and Dr. Gregory. If you have additional questions for today's speakers please email us at coca@cdc.gov.

Put Dr. Townes or Dr. Gregory's name in the subject line of your email and we will ensure that your email is forwarded to them for a response. Again that email address is c-o-c-a@cdc.gov. The recording of this call and the transcript will be posted to the COCA Website at emergency.cdc.gov forwarsslash coca within the next few days.

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Thank you again for being a part of today's COCA call. Have a great day.

Coordinator: Thank you and that does conclude today's conference.

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